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#### Amendments to the Claims:

Please amend Claims 56, 57 and 59-62, and add new Claim 148 as set forth below.

#### 1-48. (Canceled)

49. (Previously presented) A substrate for a protein kinase, wherein the substrate is selected from the group consisting of:

$$O_2C$$
  $O_2$   $OH$  FRRRRK-amide  $O$  , and

wherein F is phenylalanine, K is lysine, and R is arginine; and wherein the LINKER is selected from the group consisting of N-methyl glycine, L-proline, D-proline,

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50-55. (Canceled)

56. (Currently amended) A substrate for a protein kinase, wherein the substrate comprises:

a peptide substrate for the protein kinase, wherein the peptide comprises a serine, a threonine, or a tyrosine on a terminal end of the peptide;

at least one fluorophore, wherein a fluorophore is attached to the serine, the threonine, or the tyrosine on the terminal end of the peptide; and

a photolabile-side chain attached to the serine, the threonine, or the tyrosine on the terminal end of the peptide, wherein the photolabile side chain blocks transfer of a phosphoryl group from adenosine triphosphate to a hydroxyl moiety of the serine, the threonine, or the tyrosine so that the substrate cannot be phosphorylated by a protein kinase until the photolabile-side chain is removed from the substrate; and

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wherein the photolabile side chain comprises the structure

or a fluorophore is attached to the peptide by a linker selected from the group consisting of

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#### wherein

- (i) the substrate is specific for a protein kinase subtype,
- (ii) the fluorophore is attached to the C-terminal end of the peptide,
- (iii) a fluorophore is attached to each terminal end of the peptide,
- (iv) a first fluorophore is attached to a terminal end of the peptide and a second fluorophore, with photophysical properties distinct from the first fluorophore, is attached to any nonterminal site on the peptide,
  - (v) the fluorophore is a 7-nitrobenz-2-oxa-1,3-diazole derivative,
- (vi) the fluorophore is attached to the peptide by a linker selected from the group consisting of a carboxamide linker, an aminobenzoic acid linker, a sulfonamide linker, a urea linker, a thiourea linker, an ester linker, a thioester linker, an alkylamine linker, an arylamine linker, and a thioether linker, and/or
  - (vii) the substrate further comprises a carbohydrate, a lipid or a nucleic acid.
  - 57. (Currently amended) The substrate of claim <u>148</u>, <del>56</del>, wherein the photolabile

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side chain comprises the structure

- 58. (Original) The substrate of claim 56, wherein the substrate comprises a serine with a photolabile side chain that blocks phosphoryl transfer.
- 59. (Currently amended) The substrate of claim <u>56</u>, <del>58</del>, wherein the substrate has the structure

- 60. (Currently amended) The substrate of claim 148, 56, wherein after removal of the photolabile side chain, phosphorylation by a protein kinase of the terminal serine, the terminal threonine, or the terminal tyrosine to which the fluorophore is attached produces at least a 20% change in fluorescence intensity.
- 61. (Currently amended) The substrate of claim <u>148</u>, <del>56</del>, wherein after removal of the photolabile side chain, phosphorylation by a protein kinase of the terminal serine, the terminal threonine, or the terminal tyrosine to which the fluorophore is attached produces

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at least a 20% increase in fluorescence intensity.

62. (Currently amended) The substrate of claim <u>148</u>, <del>56</del>, wherein after removal of the photolabile side chain, phosphorylation by a protein kinase of the terminal serine, the terminal threonine, or the terminal tyrosine to which the fluorophore is attached produces at least a 20% decrease in fluorescence intensity.

at rouse a 20% decrease in madrescence intensity.

63. (Previously presented) The substrate of claim 60, wherein phosphorylation of the substrate by the protein kinase produces at least a 70% change in fluorescence

intensity.

64. (Original) The substrate of claim 63, wherein phosphorylation of the substrate

by the protein kinase produces at least a 100% change in fluorescence intensity.

65. (Original) The substrate of claim 64, wherein phosphorylation of the substrate

by the protein kinase produces at least a 150% change in fluorescence intensity.

66. (Original) The substrate of claim 65, wherein phosphorylation of the substrate

by the protein kinase produces at least a 250% change in fluorescence intensity.

67. (Previously presented) The substrate of claim 56, wherein the substrate is

specific for a protein kinase subtype.

68. (Original) The substrate of claim 67, wherein the substrate is specific for

protein kinase C.

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69. (Original) The substrate of claim 68, wherein the substrate is specific for

isoforms  $\alpha$ ,  $\beta$ , and  $\gamma$  of protein kinase C.

70. (Withdrawn) The substrate of claim 67, wherein the substrate is specific for

protein kinase A, protein kinase B, protein kinase D, protein kinase G, Ca<sup>+</sup>/calmodulin-

dependent protein kinase, mitogen-activated protein kinase, protein kinase mos, protein

kinase raf, protein tyrosine kinase, tyrosine kinase abl, tyrosine kinase src, tyrosine kinase

yes, tyrosine kinase fps, tyrosine kinase met, cyclin-dependent protein kinase, or cdc2

kinase.

71. (Previously presented) The substrate of claim 56, wherein the substrate

further comprises a carbohydrate, a lipid or a nucleic acid.

72. (Canceled)

73. (Previously presented) The substrate of claim 56, wherein the fluorophore is

attached to the C-terminal end of the peptide.

74. (Previously presented) The substrate of claim 56, wherein the fluorophore is

attached to the N-terminal end of the peptide.

75. (Previously presented) The substrate of claim 56, wherein a fluorophore is

attached to each terminal end of the peptide.

76. (Original) The substrate of claim 75, wherein fluorophores with distinct

photophysical properties are attached to different terminal ends of the peptide.

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77. (Previously presented) The substrate of claim 56, wherein a first fluorophore is attached to a terminal end of the peptide and a second fluorophore, with photophysical properties distinct from the first fluorophore, is attached to any nonterminal site on the peptide.

78. (Previously presented) The substrate of claim 56, wherein the fluorophore is a 7-nitrobenz-2-oxa-1,3-diazole derivative.

79. (Withdrawn) The substrate of claim 56, wherein the fluorophore is a fluorescein derivative.

80. (Withdrawn) The substrate of claim 56, wherein the fluorophore is selected from the group consisting of a dansyl derivative, an acridine derivative, an Alexa Fluor derivative, a BODIPY derivative, an Oregon Green derivative, a Rhodamine Green derivative, a Rhodamine Red-X derivative, a Texas Red derivative, a Cascade Blue derivative, a Cascade Yellow derivative, a Marina Blue derivative, a Pacific Blue derivative, an AMCA-X derivative, and a coumarin derivative.

#### 81. (Canceled)

- 82. (Withdrawn) The substrate of claim 56, wherein the fluorophore is attached to the peptide by a metal chelating linker.
- 83. (Previously presented) The substrate of claim 56, wherein the fluorophore is attached to the peptide by a linker selected from the group consisting of a carboxamide

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linker, an aminobenzoic acid linker, a sulfonamide linker, a urea linker, a thiourea linker, an ester linker, a thioester linker, an alkylamine linker, an arylamine linker, an ether linker, and a thioether linker.

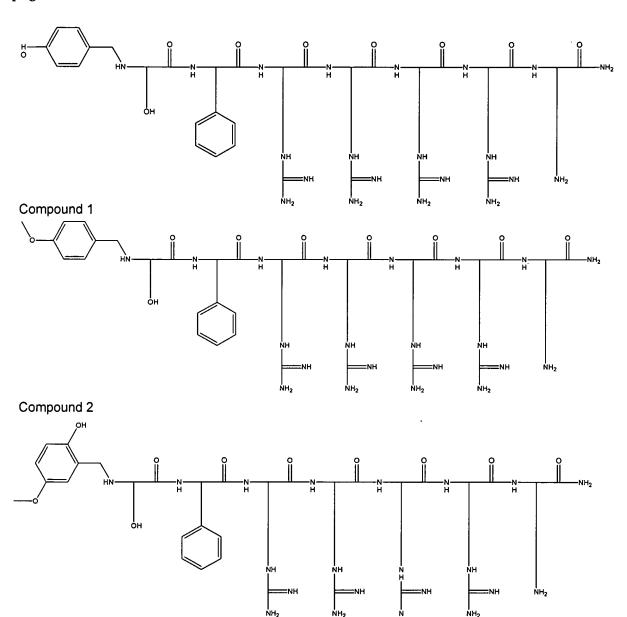
84. (Withdrawn) The substrate of claim 56, wherein the fluorophore is attached to the peptide by a linker selected from the group consisting of N-methyl glycine, L-proline, D-proline,

85. (Canceled)

- 86. (Previously presented) A composition comprising the substrate of claim 56, and a carrier.
- 87. (Original) The composition of claim 86, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.
- 88. (Previously presented) A chemical compound selected from the group of compounds consisting of:

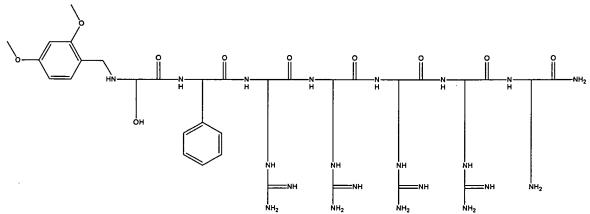
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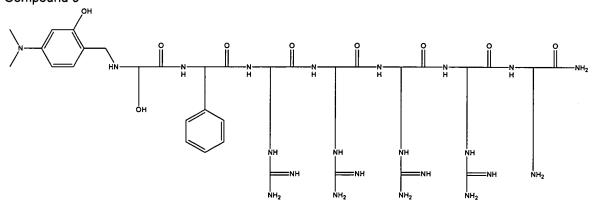
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#### Compound 4

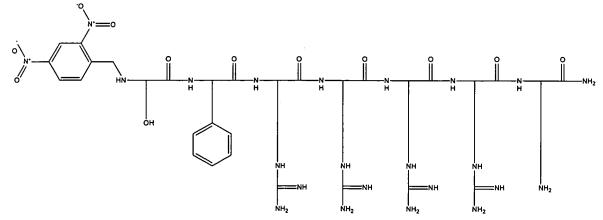
#### Compound 5



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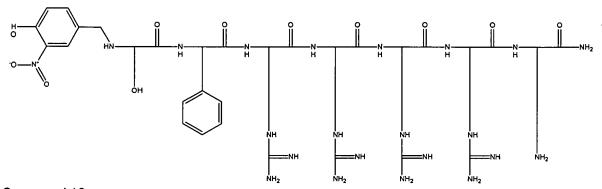
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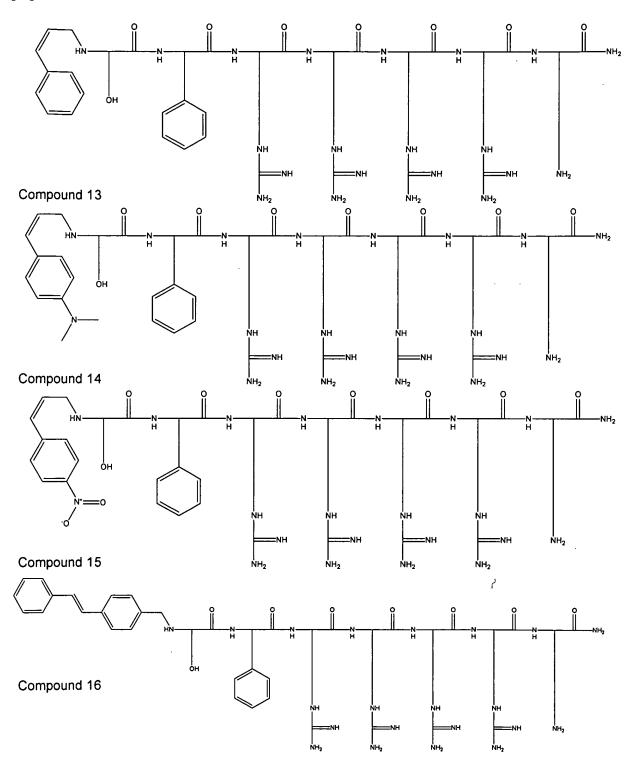


# Compound 10

## Compound 11

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#### Compound 20

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# Compound 23

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#### Compound 29

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#### Compound 35

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# Compound 37

#### Compound 38

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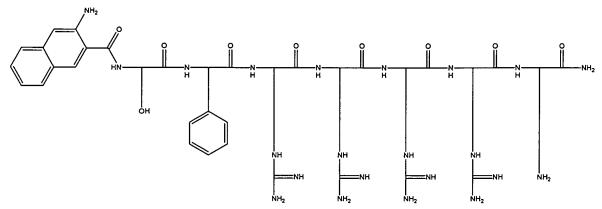
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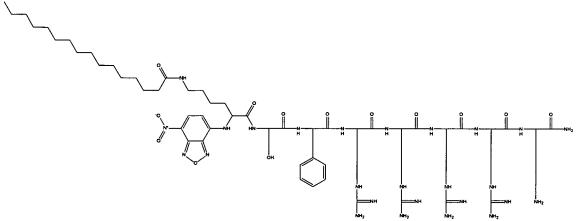
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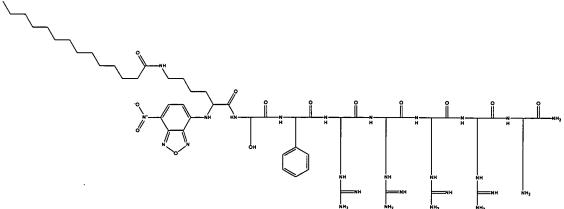
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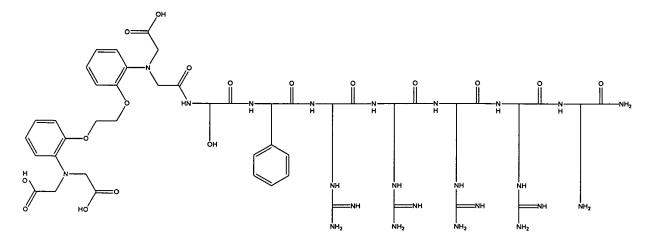




Compound 45

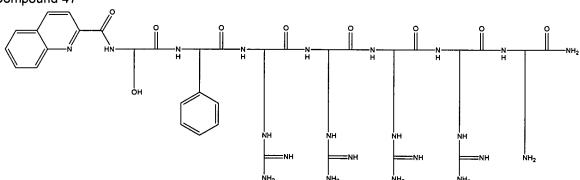
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## Compound 46

## Compound 47



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# Compound 49

#### Compound 50

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#### Compound 52

#### Compound 53

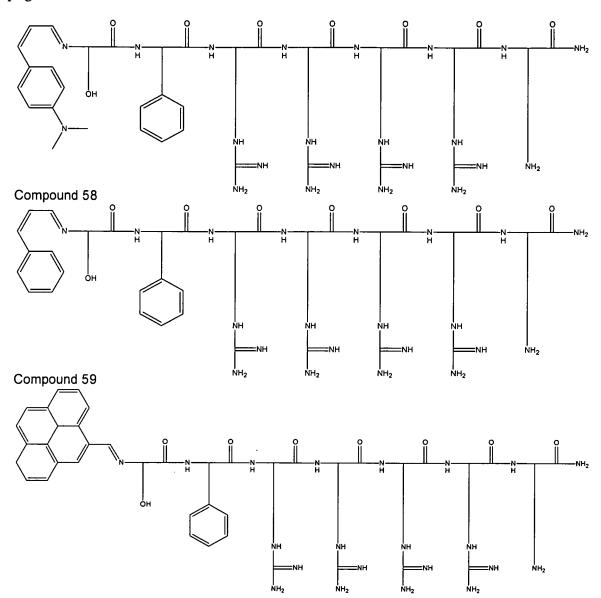
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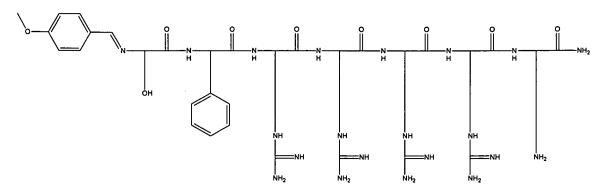
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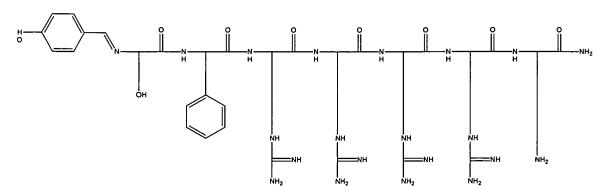


# Compound 61

#### Compound 62

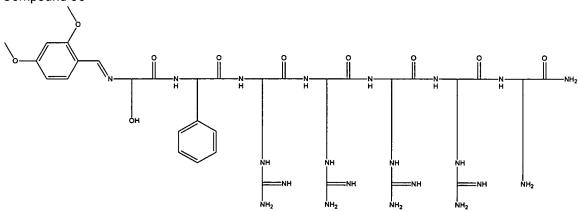
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# Compound 64

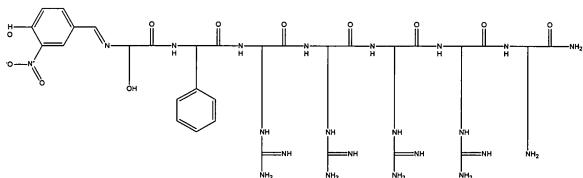
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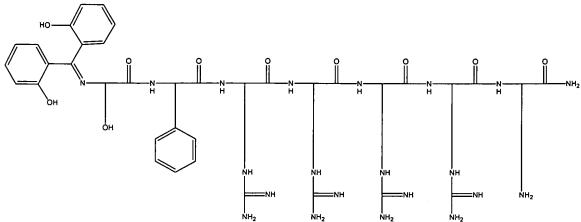
# Compound 67



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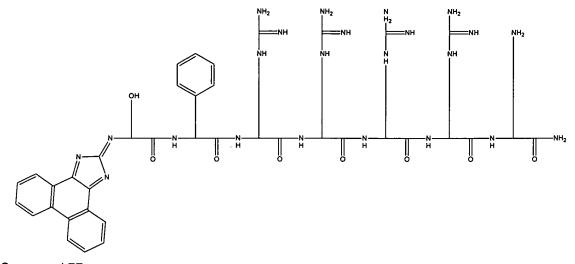
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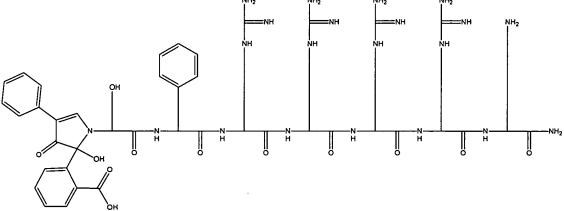
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Compound 77



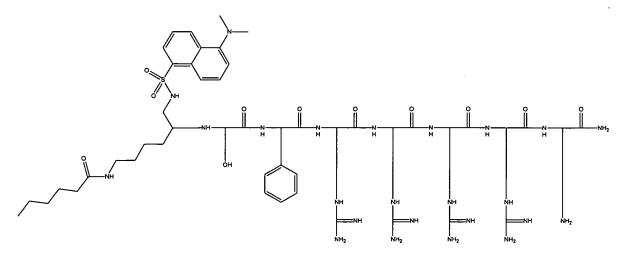
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# Compound 79

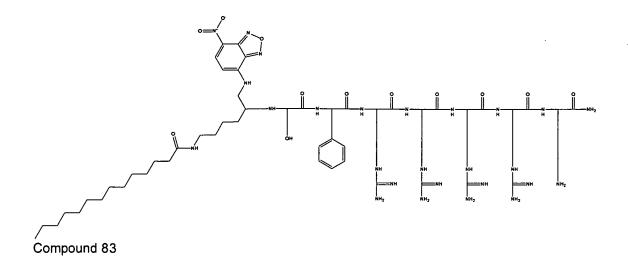
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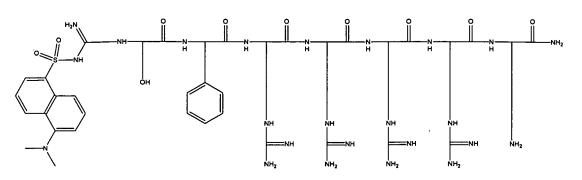


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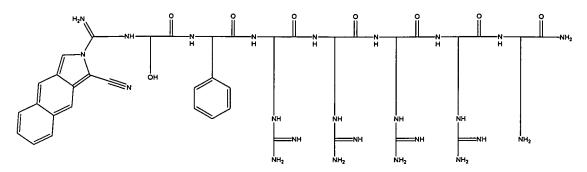
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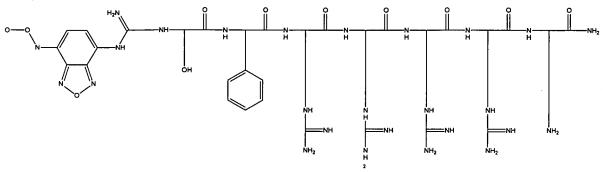


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#### Compound 86



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#### Compound 89

#### Compound 90

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I NH<sub>2</sub>

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Compound 316

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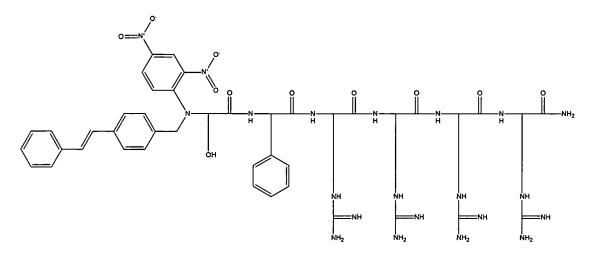
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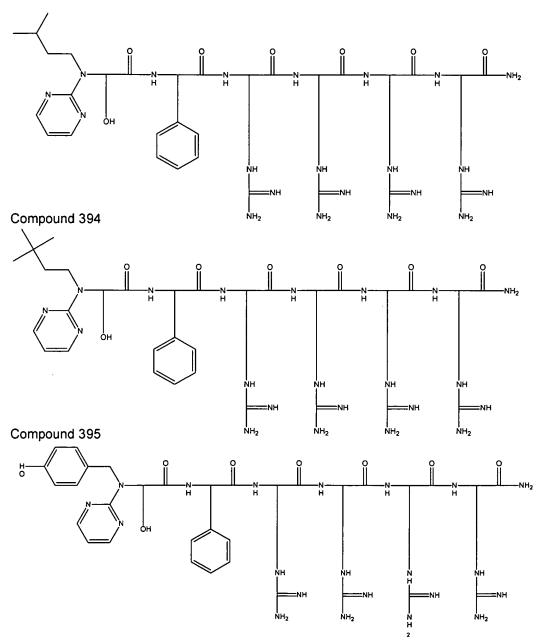
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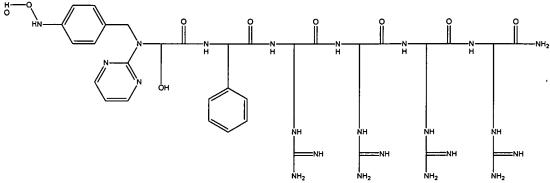


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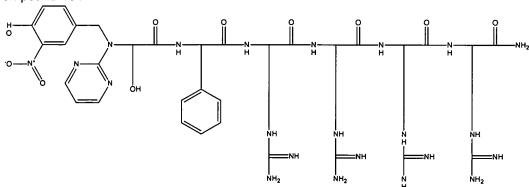
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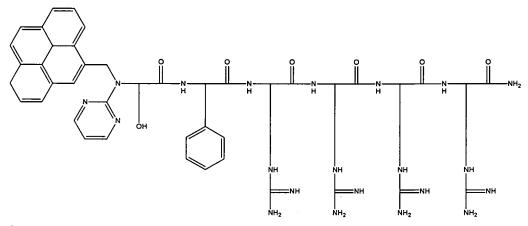
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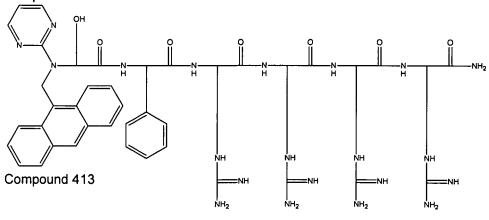
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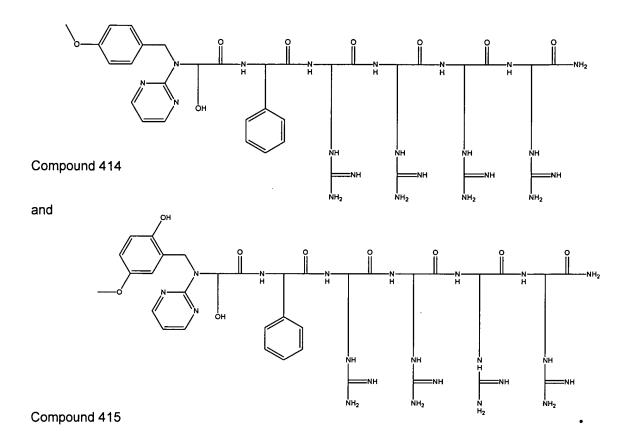


## Compound 411



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## 89. (Original) A chemical compound having the structure:

wherein the LINKER is selected from the group consisting of the following:

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90. (Original) A chemical compound having the structure:

fluorophore-LINKER-X-FRRRRK-amide (SEQ ID NO:3);

wherein F is phenylalanine; K is lysine; R is arginine; and X is serine, threonine, or

tyrosine.

91. (Original) The chemical compound of claim 90, wherein the fluorophore is a

7-nitrobenz-2-oxa-1,3-diazole derivative.

92. (Withdrawn) The chemical compound of claim 90, wherein the fluorophore is a

fluorescein derivative.

93. (Withdrawn) The chemical compound of claim 90, wherein the fluorophore is

selected from the group consisting of a dansyl derivative, an acridine derivative, an Alexa

Fluor derivative, a BODIPY derivative, an Oregon Green derivative, a Rhodamine Green

derivative, a Rhodamine Red-X derivative, a Texas Red derivative, a Cascade Blue

derivative, a Cascade Yellow derivative, a Marina Blue derivative, a Pacific Blue

derivative, an AMCA-X derivative, and a coumarin derivative.

94. (Withdrawn) The chemical compound of claim 90, wherein the linker is a

metal chelating linker.

95. (Original) The chemical compound of claim 90, wherein the linker is selected

from the group consisting of a carboxamide linker, an aminobenzoic acid linker, a

sulfonamide linker, a urea linker, a thiourea linker, an ester linker, a thioester linker, an

alkylamine linker, an arylamine linker, an ether linker, and a thioether linker.

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96. (Withdrawn) The chemical compound of claim 90, wherein the linker is selected from the group consisting of N-methyl glycine, L-proline, D-proline,

97. (Original) The chemical compound of claim 90, wherein the linker is selected from the group consisting of the following:

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- 98. (Original) The chemical compound of claim 90, wherein the chemical compound is a substrate for a protein kinase.
- 99. (Original) The chemical compound of claim 98, wherein the chemical compound is specific for protein kinase C.
- 100. (Original) The chemical compound of claim 99, wherein the chemical compound is specific for isoforms  $\alpha$ ,  $\beta$ , and  $\gamma$  of protein kinase C.
- 101. (Withdrawn) The chemical compound of claim 98, the chemical compound is specific for protein kinase A, protein kinase B, protein kinase D, protein kinase G, Ca<sup>+</sup>/calmodulin-dependent protein kinase, mitogen-activated protein kinase, protein kinase mos, protein kinase raf, protein tyrosine kinase, tyrosine kinase abl, tyrosine kinase

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src, tyrosine kinase yes, tyrosine kinase fps, tyrosine kinase met, cyclin-dependent protein kinase, or cdc2 kinase.

102. (Original) The chemical compound of claim 90, wherein the chemical compound further comprises a carbohydrate, a lipid or a nucleic acid.

103-121. (Canceled)

122. (Original) A chemical compound having the structure

$$\begin{array}{c|c} O_2N & OCH_3 \\ O_2N & O\\ O\\ N & N\\ O-N & H\\ O\end{array}$$
 Phe-Arg-Arg-Arg-Arg-Lys-amide

123. (Previously presented) A composition comprising a chemical compound of claim 89, and a carrier.

124-126. (Canceled)

- 127. (Previously presented) The substrate of claim 60, wherein the substrate comprises a metal ion chelator.
- 128. (Original) The substrate of claim 127, wherein the metal ion is a magnesium ion or a calcium ion.

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129. (Previously presented) The chemical compound of claim 90, wherein a metal ion chelator induces a change in fluorescence intensity.

130. (Original) The chemical compound of claim 129, wherein the metal ion is a magnesium ion or a calcium ion.

131. (Original) The chemical compound of claim 129, wherein the change in fluorescence intensity is at least a 20% change in fluorescence intensity.

132. (Canceled)

133. (Previously presented) The chemical compound of claim 90, wherein the linker comprises a turn to position the fluorophore in a location closer to the serine, the threonine or the tyrosine than the location the fluorophore would occupy in the absence of a turn in the linker.

134. (Previously presented) The chemical compound of claim 89, wherein the linker comprises a turn to position the fluorophore in a location closer to the terminal serine, the terminal threonine or the terminal tyrosine than the location the fluorophore would occupy in the absence of a turn in the linker.

135-136. (Canceled)

137. (Previously presented) The composition of claim 123, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically

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acceptable carrier.

- 138. (Previously presented) A composition comprising the substrate of claim 49, and a carrier.
- 139. (Previously presented) The composition of claim 138, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.
- 140. (Previously presented) A composition comprising the compound of claim 88, and a carrier.
- 141. (Previously presented) The composition of claim 140, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.
- 142. (Previously presented) A composition comprising the compound of claim 90, and a carrier.
- 143. (Previously presented) The composition of claim 142, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.

144-145. (Canceled)

146. (Previously presented) A composition comprising the compound of claim

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122, and a carrier.

147. (Previously presented) The composition of claim 146, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.

148. (New) The substrate of claim 56, wherein a photolabile side chain is attached to the serine, the threonine, or the tyrosine on the terminal end of the peptide, wherein the photolabile side chain blocks transfer of a phosphoryl group from adenosine triphosphate to a hydroxyl moiety of the serine, the threonine, or the tyrosine so that the substrate cannot be phosphorylated by a protein kinase until the photolabile side chain is removed from the substrate.